DETAILED ACTION

Status of Claims

Currently, claims 1-5 are pending and under examination on the merits in the instant application.

Claim Objections

Claim 4 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 2. Note that claims 2 and 4 are identical *verbatim.* When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and /or chemical properties, functional characteristics, structure/function correlation, or any combination thereof.

In the instant case, claims 2-5 require that an antisense oligonucleotide targeted to the translation initiation codon region or the 3'-UTR of a thymidylate synthase mRNA "increases" expression of thymidylate synthase.

With regard to the broadly claimed genus of thymidylate synthase (TS)-targeted antisense oligonucleotides, the instant specification discloses a single species: "SEQ ID NO:10" targeted to the translation initiation region of the TS gene, which results in a 70% increase in TS transcription level. See page 33. By contrast, the specification shows that "SEQ ID NO:2" targeted to the 3'-UTR of the TS gene results in a decrease in TS mRNA expression level. See page 36. As such, the instant specification clearly demonstrates that not all antisense oligonucleotides targeted to a specific region of the TS gene "increases" expression of TS, thereby presenting the unpredictability of antisense oligonucleotide activity.

In addition, it was known in the art at the time of the invention that antisense oligonucleotides bind to a target molecule and disrupts the function of the target by preventing transcription or splicing or translation. See page 7 of Schmitz et al. (WO 98/49287, applicant's citation). Even better, Schmitz et al. teach that antisense oligonucleotides targeted to the translation start region decrease the TS expression. See Tables 1 and 2; claims 1, 3, 22; Figures 1-2, 4. Hence, Schmitz et al. demonstrate that even the antisense oligonucleotides that are targeted to the translation initiation site decrease, not increase, the TS expression, unlike the

antisense oligonucleotide of SEQ ID NO:10 targeted to the translation initiation region of the TS gene disclosed in the instant specification, thereby presenting problems related to the unpredictability of antisense oligonucleotide design and its modulatory activity.

Note that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]." (emphasis added). See *Enzo Biochem*, 323 F.3d at 966, 63 USPQ2d at 1615; *Noelle v. Lederman*, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004)("[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated."). See also MPEP §2163.

In light of the above, the instant specification does not clearly allow persons of ordinary skill in the art to recognize that the inventors invented the genus of antisense oligonucleotides that "increase" TS expression claimed in the instant case. See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991), which clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (see page 1117).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Vincent et al. (WO 03/093291 A2, applicant's citation).

The claim is drawn to a method of identifying drug targets for cancer therapy comprising an antisense oligonucleotide complementary a thymidylate synthase mRNA and identifying genes with altered expression.

Vincent et al. teach a method of screening for potential drug targets for cancer therapy comprising gene expression assays using an antisense oligonucleotide targeted to a thymidylate synthase mRNA, wherein the target region includes translation initiation codon and the 3'-UTR . See pages 2-4, 8-10, 36-37; claims 38-40.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dean et al. (US 6,087,489, applicant's citation) in view of Chen et al. (*Molecular and Cellular Endocrinology,* 2001, 177:43-54).

The claims are drawn to a method of identifying drug targets for cancer therapy comprising an antisense oligonucleotide complementary to a translation initiation codon region or the 3'UTR region of a thymidylate synthase mRNA and identifying genes with altered expression, wherein the antisense oligonucleotide increases thymidylate synthase expression.

Dean et al. teach that thymidylate synthase antisense oligonucleotides targeted to the 5'-UTR, 3'-UTR, or the translation initiation coding region are useful research reagents for cancer therapy, wherein the antisense oligonucleotides are at least about 5-50 nucleotides in length. They teach that thymidylate synthase antisense oligonucleotides "modulate" thymidylate synthase expression either by inhibition or by stimulation of the expression. See columns 3-5; column 6, lines 18-22, 30-32, 62-67; column 7. Dean et al. do not teach that thymidylate synthase antisense oligonucleotides are used in a research method for identifying potential anticancer drug targets.

Chen et al. teach that one can identify and validate potential drug target molecules for drug discovery by transfecting cells with an antisense oligonucleotide and analyzing differential gene expression profiles, which show genes that are positively and negatively regulated (or modulated) by the antisense oligonucleotide. See the entire reference.

It would have been *prima facie* obvious at the time the invention was made to use the antisense oligonucleotides targeted to the translation initiation coding region or the 3'-UTR of the TS gene of Dean et al. in the drug target identification method of Chen et al.

One of ordinary skill in the art would have been motivated to combine the teachings of the prior art with a reasonable expectation of success, because the utility of anti-thymidylate synthase antisense oligonucleotides in cancer therapy research was known in the art as taught by Dean et al., and because the utility of antisense oligonucleotides in analyzing differential gene expression profiles, thereby identifying potential drug target molecules for drug discovery was known in the art as taught by Chen et al. Since Dean et al. expressly taught that anti-thymidylate synthase antisense oligonucleotides targeted to the 5'-UTR, 3'-UTR, or the translation initiation coding region can either stimulate or inhibit thymidylate synthase expression, one of ordinary skill in the art would have been motivated to use an antisense oligonucleotide that stimulates thymidylate synthase expression when identifying potential anti-cancer drug target molecules. Since all the knowledge and skills required for the claimed invention were within the technical grasp of one of ordinary skill in the art at the time of the invention, the skilled artisan would have arrived at the claimed invention with a reasonable expectation of success. Accordingly, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over DeMoor et al. (*Experimental Cell Research,* 1998, 243:11-21) in view of Chen et al. (*Molecular and Cellular Endocrinology,* 2001, 177:43-54).

The claims are described above.

DeMoor et al. teach that an antisense oligonucleotide complementary to the translation start site of TS gene significantly increases TS gene transcription and therefore TS mRNA expression. They teach that TS is an art-recognized target for cancer chemotherapeutic agents. See the entire reference. DeMoor et al. do not teach using the antisense oligonucleotide to identify potential drug targets for cancer therapy.

Chen et al. teach that one can identify and validate potential drug target molecules for drug discovery by transfecting cells with an antisense oligonucleotide and analyzing differential gene expression profiles, which show genes that are positively and negatively regulated (or modulated) by the antisense oligonucleotide. See the entire reference.

It would have been *prima facie* obvious at the time the invention was made to use the antisense oligonucleotide targeted to the translation initiation coding region of the TS gene of DeMoor et al. in the drug target identification method of Chen et al.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success, because the utility of anti-thymidylate synthase antisense oligonucleotides in cancer therapy research was known in the art as taught by DeMoor et al., and because the utility of antisense oligonucleotides in analyzing differential gene expression profiles, thereby identifying potential drug target molecules for drug discovery was known in the art as taught by Chen et al. Since DeMoor et al. expressly taught that anti-thymidylate synthase

antisense oligonucleotide targeted to the translation initiation coding region can stimulates thymidylate synthase expression, one of ordinary skill in the art would have been motivated to use the antisense oligonucleotide of DeMoor et al. when identifying potential anti-cancer drug target molecules, thereby identifying those molecules whose expressions are differentiated or modulated due to the increased expression of thymidylate synthase, one of art-recognized target for cancer chemotherapeutic agents. Since all the knowledge and skills required for the claimed invention were within the technical grasp of one of ordinary skill in the art at the time of the invention, the skilled artisan would have arrived at the claimed invention with a reasonable expectation of success. Accordingly, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 1 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 38 of copending Application No. 12/050,086. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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